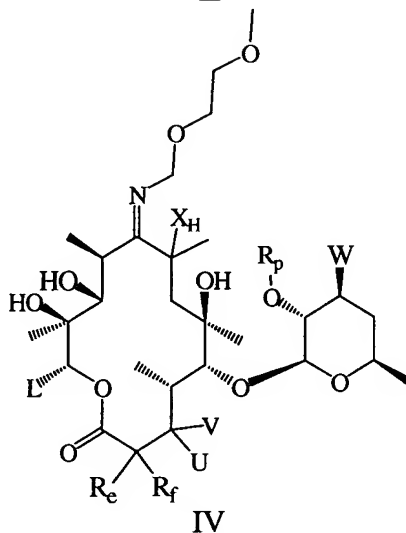
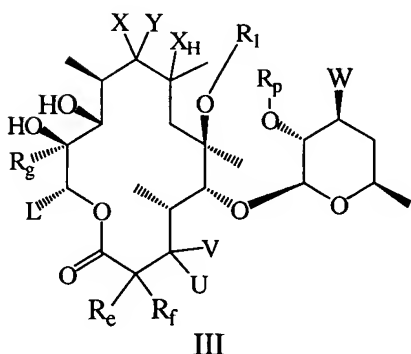
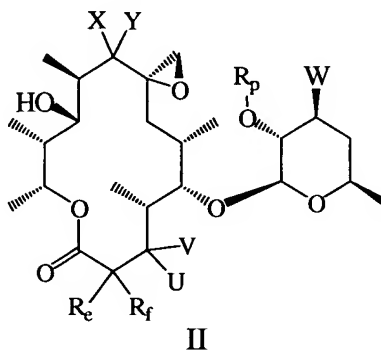
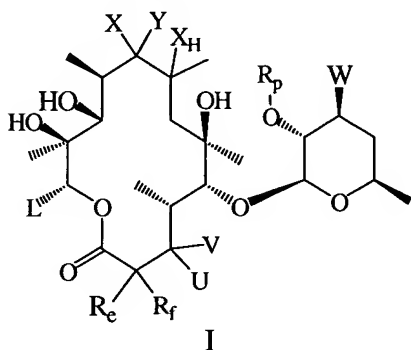
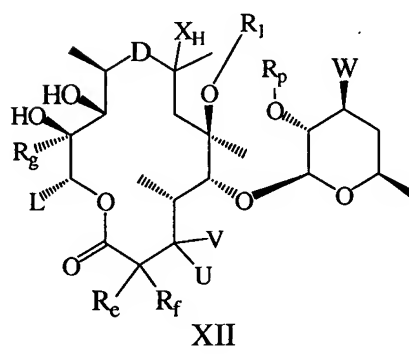
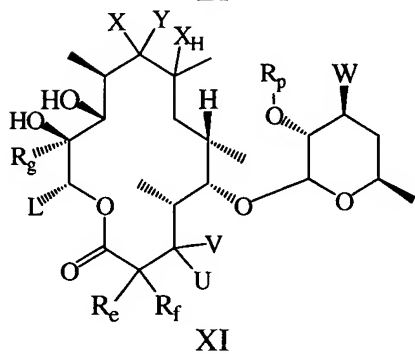
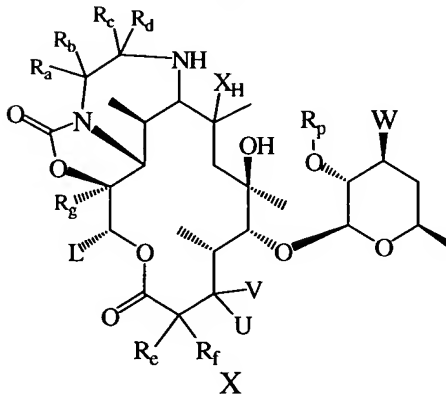
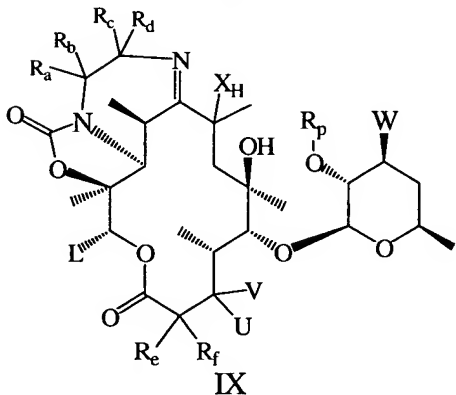
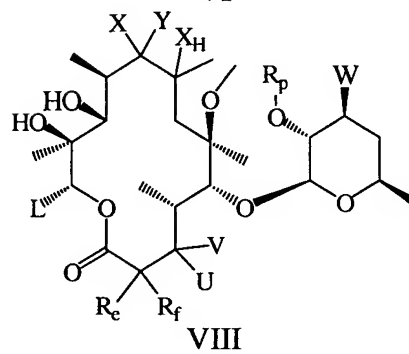
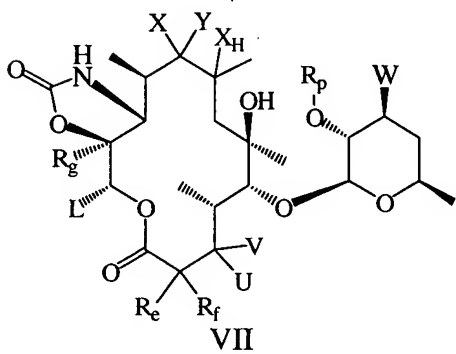
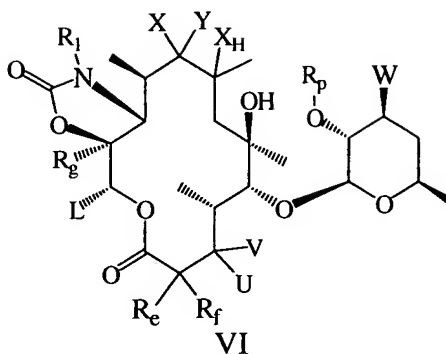
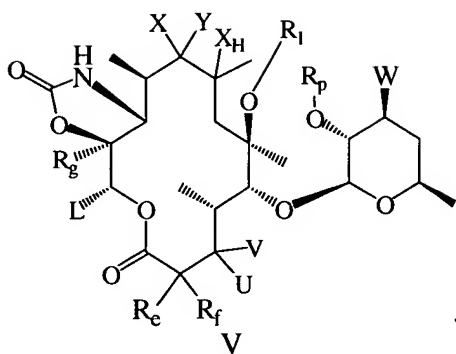
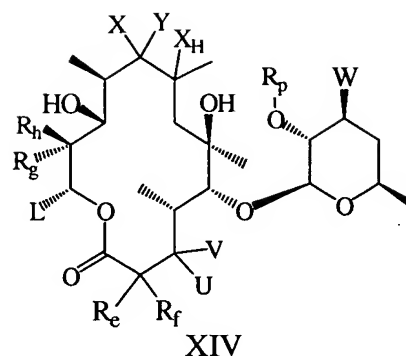
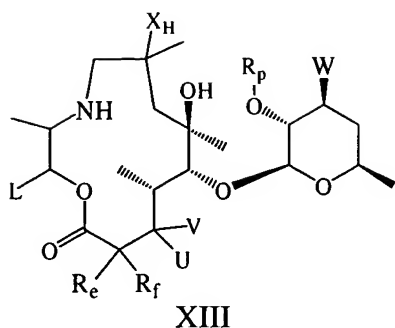


1. A process comprising the step of reacting a macrocyclic compound characterized by at least two nucleophilic moieties with a bridging component optionally in the presence of catalyst thereby achieving a bridged macrocyclic product.
2. The process of claim 1, wherein the macrocyclic compound is a macrolide antibiotic.
3. The process of claim 1, wherein the macrocyclic compound is an erythromycin derivative.
4. The process of claim 3, wherein the erythromycin derivative is azithromycin, desmethyl azithromycin, roxithromycin, clarithromycin, telithromycin, or cethromycin.
5. The process of claim 1, wherein the macrocyclic compound is selected from:







wherein

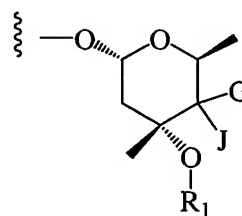
D is selected from  $-\text{NHCH}_2-$ ,  $-\text{NHCHR}_1-$ ,  $-\text{NHCR}_3\text{R}_4-$ ,  $-\text{NR}_1\text{CH}_2-$ ,  $-\text{NHC(O)}-$ ,  $-\text{NR}_1\text{C(O)}-$ ,  $-\text{NHC(S)}-$ , or  $-\text{NR}_1\text{C(S)}-$ ;

Each  $\text{R}_1$  is independently selected from hydrogen, deuterium, a substituted or unsubstituted, saturated or unsaturated aliphatic group, a substituted or unsubstituted, saturated or unsaturated alicyclic group, a substituted or unsubstituted aromatic group, a substituted or unsubstituted heteroaromatic group, saturated or unsaturated heterocyclic group;

$\text{R}_3$  and  $\text{R}_4$  is independently selected from the group consisting of hydrogen, acyl, a substituted or unsubstituted, saturated or unsaturated aliphatic group, a substituted or unsubstituted, saturated or unsaturated alicyclic group, a substituted or unsubstituted aromatic group, a substituted or unsubstituted heteroaromatic group, saturated or unsaturated heterocyclic group; or can be taken together with the nitrogen atom to which they are attached to form a substituted or unsubstituted heterocyclic or heteroaromatic ring;

L is selected from hydrogen, a substituted or unsubstituted, saturated or unsaturated aliphatic group, a substituted or unsubstituted, saturated or unsaturated alicyclic group, a substituted or unsubstituted aromatic group, a substituted or unsubstituted heteroaromatic group, or a substituted or unsubstituted heterocyclic group;

one of U or V is hydrogen and the other is independently selected from the group



consisting of:  $\text{R}_1$ ,  $\text{OR}_1$ ,  $\text{OC(O)R}_1$ ,  $\text{OC(O)NR}_3\text{R}_4$ ,  $\text{S(O)}_n\text{R}_1$ ,

carbohydrate or sugar moiety;

or U and V, taken together with the carbon atom to which they are attached, are  $\text{C=O}$ ;

or UV and  $R_e R_f$ , taken together with the carbon atoms to which they are attached, are –  
 $C(R_1)=CH-$ ;

one of J or G is hydrogen and the other is selected from:  $R_1$ ,  $OR_1$ , or  $NR_3 R_4$ ;

or J and G, taken together with the carbon atom to which they are attached, are selected  
 5 from:  $C=O$ ,  $C=NR_1$ ,  $C=NOR_1$ ,  $C=NO(CH_2)_m R_1$ ,  $C=NNHR_1$ ,  $C=NNHCOR_1$ ,  $C=NNHCONR_3 R_4$ ,  
 $C=NNHS(O)_n R_1$ , or  $C=N-N=CHR_1$ ;

$R_a$ ,  $R_b$ ,  $R_c$ , and  $R_d$  are independently selected from  $-R_1$ ,  $-OR_1$ ,  $-S(O)_n R_1$ ,  $-C(O)OR_1$ ,  $-$   
 $OC(O)R_1$ ,  $-OC(O)OR_1$ ,  $-C(O)R_1$ ,  $-C(O)NH-R_1$ ,  $-NHC(O)-R_1$ ,  $-N(R_3)(R_4)$ ,  $-NHC(O)-OR_1$ ,  $-$   
 $NHC(O)NH-R_1$ , or  $-OC(O)NH-R_1$ ;

10 or  $R_a$  and  $R_b$ ,  $R_a$  and  $R_c$ ,  $R_a$  and  $R_d$ ,  $R_b$  and  $R_c$ ,  $R_b$  and  $R_d$ , or  $R_c$  and  $R_d$ , taken together  
 with the carbon atom or atoms to which they are attached, are selected from substituted or  
 unsubstituted alicyclic or substituted or unsubstituted heterocyclic;

one of  $R_e$  and  $R_f$  is selected from hydrogen or methyl, and the other is independently  
 selected from halogen, deuterium, or  $R_1$ .

15  $R_h$  is hydroxy;

$R_g$  is selected from hydrogen, a substituted or unsubstituted, saturated or unsaturated  
 aliphatic group, a substituted or unsubstituted, saturated or unsaturated alicyclic group, a  
 substituted or unsubstituted aromatic group, a substituted or unsubstituted heteroaromatic group,  
 or a substituted or unsubstituted heterocyclic group;

20 or  $R_g$  and  $R_h$ , taken together with the carbon atom to which they are attached, are selected  
 from an epoxide, a carbonyl, a substituted or unsubstituted olefin, a substituted or unsubstituted  
 alicyclic, a substituted or unsubstituted heterocyclic;

W is  $NR_3 R_4$ ;

one of X and Y is hydrogen, substituted or unsubstituted aliphatic, and the other is  
 25 independently selected from: hydroxy,  $-SH$ ,  $-NH_2$ , or  $-NR_1 H$ ;

or X and Y, taken together with the carbon atom to which they are attached, are selected  
 from:  $C=O$ ,  $C=NR_1$ ,  $C=NOR_1$ ,  $C=NO(CH_2)_m R_1$ ,  $C=NNHR_1$ ,  $C=NNHCOR_1$ ,  $C=NNHCONR_3 R_4$ ,  
 $C=NNHS(O)_n R_1$ , or  $C=N-N=CHR_1$ ;

$R_p$  is selected from hydrogen, acyl, silane, or a hydroxy protecting group;

30  $X_H$  is selected from hydrogen or halogen;

m is an integer; and

n is 0, 1, or 2.

6. The process of claim 4, wherein, for the macrocyclic compound, L is ethyl.
7. The process of claim 4, wherein, for the macrocyclic compound, one of X and Y is hydrogen and the other is selected from hydroxy or amino.
- 5 8. The process of claim 4, wherein, for the macrocyclic compound, X and Y, taken together with the carbon atom to which they are attached, are selected from C=O, C=NH, C=N-OH, or C=N-NH<sub>2</sub>;
9. The process of claim 4, wherein, for the macrocyclic compound, R<sub>g</sub> is methyl.
- 10 10. The process of claim 4, wherein, for the macrocyclic compound, R<sub>e</sub> is hydrogen and R<sub>f</sub> is selected from methyl, allyl, or propargyl.
11. The process of claim 4, wherein, for the macrocyclic compound, one of U and V is hydrogen and the other is selected from -OH or -O-cladinose.
12. The process of claim 4, wherein, for the macrocyclic compound, U and V, taken together with the carbon atom to which they are attached, are C=O.
- 15 13. A bridged macrocyclic product produced by the process of claim 1.